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(54) Disinfecting and cleaning composition.

(57) A disinfection solution, primarily for use in conjunction with contact lenses is disclosed comprising an amount of a pharmaceutically acceptable ionic salt which is equivalent in ionic strength to at least 5 % w/v sodium chloride, at least one of a C_{2-6}alkanol and a C_{3-8}alkylene glycol, a pharmaceutically acceptable surfactant, optionally a buffer and a viscosity enhancing agent, and water.

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HIGH SALT CONTENT RAPID DISINFECTION SOLUTION FOR CONTACT LENSES

The invention is in the area of contact lens care products, particularly solutions used to clean and disinfect contact lenses.

Disinfection solutions for use in conjunction with contact lenses have been in use essentially as long as contact lenses have been available to the public. There is a large diversity in the makeup of the various known solutions, primarily due to the fact that to date no single solution has been found to meet all of the parameters desired in a single solution. For example, currently commercially available solutions such as ReNu Disinfectant (Bausch & Lomb), Optisoft (Alcon), and Optifree (Alcon) which offer low irritancy and/or hypersensitivity require a minimum of four hours soaking to disinfect. Solutions such as Flexcare contain thimerosol which has been particularly problematical as a disinfecting or preservative agent. Because of these problems there has been an attempt to avoid thimerosol as an antimicrobial agent.

A second, and not small consideration, is contact lens material/solution compatibility. Heat disinfection is not a practical alternative for use with high water content soft contact lenses. Some lenses entrap or react with various components of the disinfection solution making it impossible to utilize such solutions with those lenses. For this reason, proper patient compliance with lens/solution match-up directions is essential to maintaining contact lenses properly. Yet experience has shown that patient compliance with lens and solution manufacturer directions is not adhered to by a significant, although small patient population. Hence, there has been an effort to develop a disinfection solution which is generally useful for most, if not all contact lenses currently available.

Finally, not all disinfectant solutions are suitably effective against the entire range of microbial organisms which are of concern in the contact lens field. One such organism where disinfectants and preservatives have had limited success is Acanthamoeba. The present invention solution is effective against the cyst as well as the trophozite stage of these protozoa.

One object of the invention is to provide a contact lens disinfecting solution which will be non-irritating to the patient after following a simple, easy to carry out disinfecting regimen.

A second object of the invention is to provide a one step cleaning and disinfecting solution meeting the foregoing object.

A third object is to provide a contact lens disinfection solution having compatibility with essentially all currently available contact lenses.

A fourth object of the invention is to provide a disinfection solution which is effective against a wide range of ocular pathogens including Acanthamoeba.

Surprisingly, the foregoing objects and others are achieved by a disinfection solution comprising

a) at least one of a C_{2-6}alkanol and a C_{3-8}alkylene glycol;

b) an amount of a pharmaceutically acceptable contact lens compatible salt which is sufficient to raise the solution tonicity at least to the equivalent of a 5 % sodium chloride solution;

c) optionally a pharmaceutically acceptable contact lens compatible amphoteric surfactant;

d) optionally a pharmaceutically acceptable contact lens compatible pH regulating agent or buffer;

e) optionally a pharmaceutically acceptable contact lens compatible viscosity enhancing agent; and

f) the balance of a suitable solvent which is preferably water.

It should be emphasized here that the invention is also applicable beyond the contact lens disinfection and preservative field and may be used anywhere a disinfecting solution treatment or preserved solution would be useful provided only that the subject material to be treated is not adversely affected by the solution components. For these purposes, the invention solution need not be contact lens compatible or even pharmaceutically acceptable. The only important features in such a case are that the solution contain a tonicity building agent in an amount equivalent to a 5 % or more concentrated solution of sodium chloride and at least one of (aa) a C_{2-6}alkanol and (ab) a C_{3-8}alkylene glycol. Typical non-contant lens disinfecting applications for which such solutions are useful include: lens case cleaner and disinfectant, topical medical composition, cosmetic, facial cleaner, hand cleaner, disinfecting soaps such as surgical soap, shampoo, household disinfectant, and industrial disinfectant, laboratory disinfectant, dental and medical equipment disinfectant, acne cleaning and disinfecting treatments, insect bite disinfection, for minor skin itching and rashes and wound healing applications. It is also suitable as a rapid in-office contact lens disinfecting/cleaning regimen.

In its broadest sense, the instant invention is a disinfection solution comprising at least three components:

(a) at least one of a C_{2-6}alkanol and a C_{3-8}alkylene glycol;

(b) a tonicity building agent in an amount such that the invention solution would have a tonicity

equivalent to that of a 5 % or more concentrated aqueous sodium chloride solution; and

(f) an appropriate solvent.

Additional components which may be present include a surfactant (for enhanced cleaning capability and some antimicrobical effect if a quaternary ammonium compound); a pH regulator; and a viscosity builder. Other components may also be present which are typical for the type of formulation useful for the purpose to which the inventive solution is being put. Hence if the solution is to be a cleanser where surface scratching is not of concern, agents such as silicon dioxide may be present as well.

More specifically, the invention is directed to a disinfecting and cleaning composition comprising

a) x % by weight of a C_{3-8}alkylene glycol, and

y % by weight of a C_{2-6}alkanol

wherein x and y each independently are zero to about 50 with the proviso that $x/10 + y/2 \geq 1.0$;

b) an amount of a tonicity builder sufficient to raise the solution tonicity to at least the equivalent of a 5 % by weight sodium chloride solution;

c) 0 % to about 25 % by weight of a compatible surfactant;

d) 0 % to about 2 % by weight of a pH adjusting or regulating agent;

e) 0 % to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent; and

f) the balance of a suitable solvent which is preferably water.

The above composition preferably comprises 0 % to about 15 % of compound c) and has y % by weight of a C_{2-6}alkanol present wherein y is zero to about 30.

The formulations of the invention are typically used by contacting the surface to be treated with the formulations, rubbing up the formulation on the surface from 5-30 seconds and rinsing the treated surface. In terms of the preferred use, contact lens disinfection, the solution is placed on the lens in the same manner as any other cleaner or disinfectant for contact lenses, rubbed lightly for 5-30 seconds and rinsed with water or normal saline as appropriate.

In the typical formulation of the invention, the C_{3-8}alkylene glycol is present from about 10 % to about 50 % by weight, preferably about 15 % to about 40 % by weight, still more preferably about 17 % to about 25 % by weight, most preferably about 21 % by weight of the entire formulation.

The C_{3-8}alkylene glycol is preferably selected from 1,2 or alpha,omega glycols such as 1,2-propylene glycol, 1,2-butylene glycol, 1,2-pentylene glycol, 1,2-hexylene glycol, 1,3-propylene glycol, 1,4-butylene glycol, 1,5-pentylene glycol, and 1,6-hexylene glycol. Also preferably, the C_{3-8}alkylene glycols are C_3 or C_4 alkylene glycols such as 1,2-propylene glycol, 1,3-propylene glycol, 1,2-butylene glycol, 1,3-butylene glycol, 1,4-butylene glycol, 2,3-butylene glycol, 2-methyl-1,2-propylene glycol, and 2-methyl-1,3-propylene glycol. Most preferably, the C_{3-8}alkylene glycol is 1,2-propylene glycol or 1,3-propylene glycol. Another highly preferable glycol is 1,6-hexylene glycol.

The lower alkanol, when present, may be used in amounts up to about 50 % by weight, but usually is present from about 2 % to about 30 % by weight, preferably about 10 % to about 20 % by weight, most preferably about 16 % by weight of the entire formulation. Lower alkanol is selected from C_{1-7}, preferably C_{1-4}, straight or branched alkanols, such as methanol, ethanol, n-propanol, isopropanol, n-butanol, sec-butanol and t-butanol, more preferably isopropanol or ethanol, most preferably isopropanol.

When both the glycol and alkanol components are present, they may individually be present in amounts below the foregoing minimums provided that the sum of the % fraction of the two totals at least 1.0. The % fraction is defined as the actual % present divided by the minimum % previously stated (10 % for the glycol and 2 % for the lower alkanol). For example, a solution having 1 % alkanol has a % fraction of 0.5 (1 %/2 %) for alkanol. Such a solution would then require at least a % fraction of glycol of 0.5, or at least 5 % glycol component in the solution. Similarly a 1 % glycol containing solution, having a % fraction of 0.1 (1 %/10 %), would require at least an alkanol % fraction of 0.9, or 1.8 % alkanol. Simply put, if the glycol is present in x % and the alkanol y %, then the minimums of the ranges would be the solutions for the equation

$$\frac{y\ \%}{\text{minimum of alkanol alone}} + \frac{x\ \%}{\text{minimum of glycol alone}} \geq 1.0.$$

The tonicity builder is present in an amount which raises the solution tonicity to at least the equivalent of a 5 % sodium chloride solution (w/v %), preferably to a tonicity in the range of 5.0 % to 20 % sodium chloride, preferably in the range of 8.5 % to 17.5 % sodium chloride, more preferably about 10 % to 15 %

sodium chloride, most preferably about 12.5 % sodium chloride. The most preferable compound for use as a tonicity builder is sodium chloride, although any compatible (ocularly compatible if ophthalmic device disinfection is the intended usage) inorganic or organic salt which does not interfere with the other components will do.

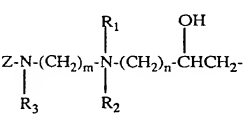
The overall solution tonicity should preferably be at least equivalent to 7.5 % to 12.5 %, more preferably about 10 % aqueous NaCl. The tonicity builder amounts required can be adjusted by those of ordinary skill to have the solution meet these overall more preferable limits. Typical tonicity builders include ophthalmically acceptable alkaline metal or alkaline earth metal halide, phosphate, carbonate, sulfate, etc. The most preferred tonicity builder is sodium chloride.

The surfactant may be present in an amount of from 0 to about 25 % by weight but, is usually present in an amount of about 2 % to about 15 % by weight, preferably about 3 % to about 12 % by weight, most preferably about 5 % by weight to about 10 % by weight of the entire formulation. However, less than 2 % may also be used. The surfactant is selected from virtually any ocularly acceptable surfactant including non-ionic, anionic, and amphoteric surfactants, and furthermore, if the ultimate use is not ophthalmic, the components need not be pharmaceutically acceptable. However, it is preferably selected from

ca) compounds of formula I

$(AmSur\text{-}O)_3\text{-}P=O$ (I)

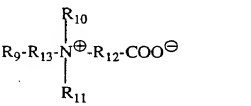
wherein the group AmSur is of the formula



(IA)

wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is an alkanoyl of 6-18 carbon atoms or Z together with R_1 and R_2 is a carbon substituted by C_{5-17}alkyl; and n and m are each independently 1 to 4. Where AmSur contains a net charge, a suitable ocularly acceptable counter ion, such as a halogenide, e.g. chloride, is also present in an appropriate amount. The three AmSur radicals can be the same or different, but preferably all three AmSur radicals in one molecule are the same;

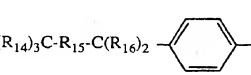
cb) compounds of the formula



(VII)

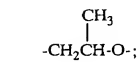
wherein R_9 is alkyl of 5-17 carbon atoms or a C_{6-20}alkanoylamino; each of R_{10} and R_{11} is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl; R_{12} is an alpha,omega-alkylene of 1 to 6 carbons which is unsubstituted or substituted by lower alkyl, hydroxy, or hydroxy lower alkyl; and R_{13} is alpha,omega-C_{1-5}alkylene;

cc) compounds of the formula



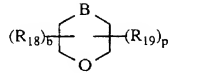
(VIII)

wherein each R_{14} and each R_{16} is independently C_{1-4}alkyl; R_{15} is C_{1-4}-alpha,omega-alkylene; each R_{17} is independently $-CH_2CH_2O-$, $-CH_2CH_2CH_2O-$, or



and a is 3-18; and

cd) compounds of the formula



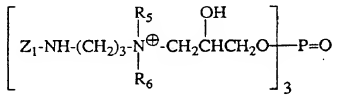
(IX)

wherein B is a C_{1-4}-alpha,omega-alkylene; p is an integer from 0 to (d-1); b is an integer which is (d-p-1); d is 4 to 7; each R_{18} is independently H or a C_{1-4}alkyl which is unsubstituted or substituted by at least one R_{19}; each R_{19} is independently hydroxy which is free, etherified by R_{20}, or esterified by R_{21}; each R_{20} is a C_{2-4} straight or branched oxyalkylene or poly(C_{2-4} straight or branched oxyalkylene), the terminal oxygen of which is bound to H or R_{21}; and each R_{21} is independently an acyl of a C_{2-24}alkanoic acid or a C_{4-24}alkenoic acid; provided that in each compound of formula IX there is at least one free hydroxy group, and at least one R_{21} group. Compounds of formula VII are typically available from Miranol under the names Mirataine® and Miranol®; compounds of formula VIII are available under the names Igepal CA®, Polytergent® and Triton X®; and compounds of formula IX are available under the Span® and Tween® brand names.

Hereinbefore and hereinafter "lower", such as in lower alkyl, refers to residues having up to 7 carbon atoms, preferably up to 4 carbon atoms.

Preferably the compounds of formula I are selected from

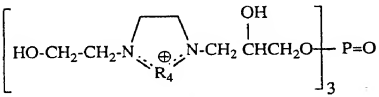
caa)



(II)

wherein R_5 and R_6 are each C_{1-4}alkyl and Z_1 is C_{6-18}alkanoyl;

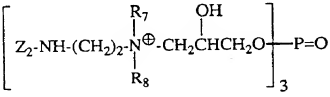
cab)



(III)

wherein R_4 is a carbon substituted by C_{5-17}alkyl and the dotted lines indicate that there is one double bond between R_4 and one of the nitrogens attached to R_4; and

cac)



(IV)

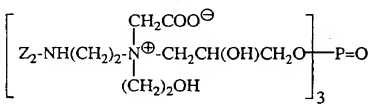
wherein Z_2 is C_{12-14}alkanoyl, one of R_7 and R_8 is carboxy lower alkyl, and the other of R_7 and R_8 is hydroxy lower alkyl.

Compounds of formulae II-IV are available from Mona Industries, New Jersey under the series trade name Monaquat®-P. More preferably, within formulae II-IV, are the compounds

caaa) $[Z_1\text{-NH-}(CH_2)_3N^{\oplus}(CH_3)_2\text{-}CH_2CH(OH)CH_2O]_3\text{-}P=O\cdot 3Cl^{\ominus}$ (V) wherein Z_1 is C_{6-17}-alkanoyl (available under the name Monaquat®P-TC) or C_{12-14}alkanoyl (available under the name Monaquat®P-TD);

caba) compounds of formula III, available under the name Monaquat®P-TZ; and

caca)



(VI)

wherein Z_2 is C_{12-14}alkanoyl, available under the name Monaquat®P-TL. The most preferable compound of the Monaquat®P series for use in the instant invention is Monaquat®P-TL, i.e. compounds of formula VI. Compounds within formula II generally are disclosed in US Patents 4,209,449 and 4,336,385, the disclosures of which are included herein by reference.

Another preferred class of surfactants includes poloxamers, reverse poloxamers, meroxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycol-buteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, ceteareths, NTA salts, EDTA salts, and pentetate salts.

Within this group, especially useful are:

poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 288, 331, 333, 334, 335, 338, 401, 402, 403 and 407;

meroxapols 105, 108, 171, 172, 174, 178, 251, 252, 254, 255, 258, 311, 312, and 314;

poloxamines 304, 504, 701, 702, 704, 707, 901, 904, 908, 1101, 1102, 1104, 1107, 1301, 1302, 1304, 1307, 1501, 1502, 1504, and 1508;

polyethylene glycols selected from PEGs 4, 6, 8, 12, 20, 32, 40, 75, 150, and PEG 6 methyl ether;

polypropylene glycols selected from PPGs 9, 12, 17, 26, and 30;

polypropylene glycol-buteths selected from ppg-5-buteth-7, ppg-7-buteth-10, ppg-12-buteth-16, ppg-20-buteth-30, ppg-28-buteth-35, and ppg-33-buteth-45;

ppg-26-oleate;

ppg-6-pareth;

tetrahydroxypropylethylenediamine;

ceteareth 27 and 55;

trisodium NTA;

trisodium EDTA and tetrasodium EDTA;

EDTA; and

pentasodium pentetate. Each of these compounds can be found in the C.T.F.A. Ingredient Dictionary.

The pH regulating component, when present, can be added as a preformed buffer or can be formed in situ. If the pH of the solution without this component is suitable it is not required, although its presence is desirable. Any ocularly compatible inorganic or organic acid or base or buffer system can be used. Typical buffer systems include the well known phosphate or borate systems. Other suitable organic buffer systems include, without limitation, the lactate, pyruvate, citrate, tartrate, acetate, and laurate systems. Preferably said pH adjusting or regulating agent is selected from i) phosphoric acid, boric acid, lactic acid and citric acid, ii) an ophthalmically acceptable salt thereof, iii) a mixture of said acid and said salt of said acid, iv) an ophthalmically acceptable inorganic acid and v) an ophthalmically acceptable inorganic base.

Most preferably the buffer system used will have a pK in the range of the desired pH range so as to maximize the buffering capacity. The most preferable buffer system is lactic acid/lactate which is preferably formed in situ by the addition of lactic acid alone. In the case of lactic acid/lactate as the pH adjuster (i.e. buffer), the combined lactic acid and lactate are preferably present from about 0.5 to about 2 % by weight of the solution based on lactate ion, more preferably about 0.75 % to about 1.5 %, most preferably about 1.1 % of the solution.

The pH of the final solution may be advantageously in the range of 3 to 7.0, preferably 5 to 7, more preferably about 5.5 to about 6. The lower pHs, while suitable, are advantageous in that minimum

disinfecting time is shortened over the same composition at higher pH, but disadvantageous that reestablishment of neutral pH is necessary before a lens is placed back on the eye.

The viscosity enhancer, when present, is present to help increase the solution viscosity to preferably not greater than 100 cps, more preferably not greater than 80 cps, still more preferably not greater than 30 cps, most preferably not greater than 10 cps. Any ocularly compatible non-ionic or quaternary ammonium viscosity enhancer is suitable. Examples of non-ionic viscosity enhancers utilizable on the instant invention include: lower alkyl celluloses (i.e. methyl cellulose, ethyl cellulose, etc.) hydroxy lower alkyl celluloses (i.e. hydroxy methyl cellulose, hydroxy ethyl cellulose, hydroxy propyl cellulose, etc.), hydroxy-lower alkanoyl cellulose, lower alkanoyl cellulose, and carboxy-lower alkyl-cellulose, poloxamers, reverse poloxamers, ethoxylated ethylene diamines, etc.

Preferably, the viscosity enhancer is a cellulose ether, more preferably hydroxy lower alkyl cellulose, most preferably hydroxy ethyl cellulose, such as HECQP 4400 available from Union Carbide. In a most preferred solution, hydroxy ethyl cellulose is the viscosity enhancer and is present in an amount of about 0.1 % by weight of the solution.

Another preferred class of viscosity enhancing agents includes poloxamers, reverse poloxamers, meroxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, poly propyleneglycol-buteths, poly-propyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, ceteareths, NTA salts, EDTA salts, and pentetate salts. Within this group, especially useful are:
poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 288, 331, 333, 334, 335, 338, 401,402, 403, and 407;
meroxapols 105, 108, 171, 172, 174, 178, 251, 252, 254, 255, 258, 311, 312, and 314;
poloxamines 304, 504, 701, 702, 704, 707, 901, 904, 908, 1101, 1102, 1104, 1107, 1301, 1302, 1304, 1307, 1501, 1502, 1504, and 1508;
polyethylene glycols selected from PEGs 4, 6, 8, 12, 20, 32, 40, 75, 150, and PEG 6 methyl ether;
polypropylene glycols selected from PPGs 9, 12, 17, 26, and 30;
polypropylene glycol-buteths selected from ppg-5-buteth-7, ppg-7-buteth-10, ppg-12-buteth-16, ppg-20-buteth-30, ppg-28-buteth-35, and ppg-33-buteth-45;
ppg-26-oleate;
ppg-6-pareth;
tetrahydroxypropylethylenediamine;
ceteareth 27 and 55;
trisodium NTA;
trisodium EDTA and tetrasodium EDTA;
EDTA; and
pentasodium pentetate. Each of these compounds can be found in the C.T.F.A. Ingredient Dictionary.

The solution of the invention can be formulated from the above components in any manner known in the art. For example the solid components can be dissolved directly in the water, either simultaneously or sequentially, with liquid components being added thereto either before or after the solid components. Alternatively the solid components can be triturated with one or more non-water liquid components and this mixture diluted with an appropriate amount of water. It is preferable to dissolve all of the components (other than the viscosity enhancer) first and then mix the viscosity enhancer into this solution. Variations of the above will be apparent to the ordinarily skilled formulator.

The instant solutions are rapid cleaning and disinfecting solutions for a wide range of contact lens and other materials. Typically, one applies a few drops of the solution to the lens material and rubs it for 5 to 30 seconds, preferably 10 to 20 seconds, more preferably about 15 seconds. This is repeated for the opposite surface. The lens is then rinsed in water or normal saline for at least 5 seconds, preferably 10 to 20 seconds, most preferably 15 seconds, and stored in normal saline for at least 20 seconds, preferably 30 seconds to 1.5 minutes, most preferably about 1 minute. Longer storing times are acceptable, but not necessary. The instant solution can be used in the above method for all types of contact lenses; soft lenses, hard lenses, and rigid gas permeable lenses. Such lens materials for which the instant solution can be used include bufilcon A, cabufocon A, crofilcon A, deltafilcon A, deltafilcon B, dimefilcon A, droxifilcon, etafilcon A, hefilcon A, hefilcon B, itafocon A, lidofilcon A, mafilcon A, ocufilcon A, ocufilcon B, optacryl 60, pasifocon A, pasifocon B, pasifocon C, perfilcon A, phemfilcon A, polymacon, porofocon B, silafilcon A, silafocon A, tefilcon, tetrafilcon A, vifilcon A, PMMA, silicone/MMA copolymer, MMA/glyceryl methacrylate copolymer, and poly t-butyl styrene. Others will be apparent to those of ordinary skill.

Having fully described the invention, the following Examples are presented to exemplify but do not limit the invention.

Example 1:

15.72 g isopropyl alcohol, 10.00 g of sodium chloride, 10.00 g of Pluronic F-127 (poloxamer 407), and 15.00 g of Miranol H2M (concentrate having approximately 50 % solid) are dissolved in 49.3 g of water (deionized) and the pH is adjusted with concentrated HCl to result in a solution according to the invention having a pH of 6.0. Microbiological data is presented in example 32.

Example 2:

Example 1 is followed except that the amount of Miranol H2M is 20.00 g and water is 44.3 g. Microbiological data is presented in Table 5.

Examples 3 through 16:

Examples 3-16 are prepared in the same manner as example 1 but using the amounts set forth in Table 1 below. In each of these examples, 15.7 g of isopropyl alcohol is employed and the pH is 6.0. Microbiological data is presented in Table 5.

Table 1:

Example No.	NaCl (g)	Pluronic F-127 (g)	Miranol H2M (g)	H_2O (g)
3	10.0	5.0	10.0	59.3
4	10.0	5.0	15.0	54.3
5	10.0	5.0	20.0	49.3
6	7.0	15.0	10.0	52.3
7	7.0	15.0	15.0	47.3
8	7.0	15.0	20.0	42.3
9	7.0	10.0	10.0	57.3
10	7.0	10.0	15.0	52.3
11	7.0	10.0	20.0	47.3
12	7.0	5.0	10.0	62.3
13	7.0	5.0	15.0	57.3
14	7.0	5.0	20.0	52.3
15	5.0	15.0	10.0	54.3
16	10.0	15.0	10.0	49.3

Examples 17-19:

Examples 17 to 19 are prepared in accordance with example 1 except that 16 g of isopropyl alcohol are used, the pH is 6.0 and the amounts set forth in Table 2 are employed.

Table 2:

Example No.	NaCl (g)	Pluronic F-127 (g)	Miranol H2M (g)	H_2O (g)
17	12.0	10.0	10.0	52.0
18	12.0	15.0	10.0	47.3
19	10.0	10.0	10.0	49.3

Example 20:

Example 20 is the same as example 19 except the amount of isopropyl alcohol is 20 g.

Examples 21-23:

Examples 21 to 23 are prepared in accordance with example 1 using hexylene glycol in place of the Miranol H2M. 1 g of Pluronic L-31 and 2 g of lactic acid are used and pH is 3.0 in place of the pluronic, acid, and pH in example 1. The remaining ingredients are used in the amounts shown in Table 3.

Table 3:

Example No.	Isopropyl Alcohol (g)	NaCl (g)
21	20	10
22	30	10
23	40	10

Examples 24-31:

Examples 24-31 are prepared in accordance with example 1 except that 1 g Betaine, with or without hexylene glycol as stated in Table 3 is used in place of the Miranol H2M and lactic acid (2 g) is used in place of hydrochloric acid and the pH is 3.0. 10 g of Pluronic F 127 is present in each of examples 24-31. The remaining ingredients are set forth in Table 4. The solutions are adjusted to 100 g by the addition of water:

Table 4:

Example No.	Hexylene Glycol (g)	Isopropyl Alcohol (g)	NaCl (g)
24	0	20	10
25	0	30	10
26	0	40	10
27	30	10	10
28	30	0	12
29	30	0	10
30	0	20	12
31	0	30	12

Example 32:

The solutions of examples 1 to 16 are tested for their effectiveness against S. epidermidis as follows: The organism is cultured to a density of 10^8/ml in nutrient broth. 0.01 ml of this inoculum is pipetted onto each side of a vifilcon A (55 % water) soft contact lens and left in contact therewith for 5 minutes. The inoculated lens is then allowed to soak in 2 ml of each of the solutions tested for 0.5 to 1 minute and the number of remaining viable organisms is determined. The results are reported in Table 5 below.

Table 5:

Solution of Example	No. of Surviving Viable Organisms (S. epidermidis)	% Reduction in contamination
1	5.45×10^2	99.94 %
2	8.65×10^2	99.91 %
3	0	100 %
4	50	99.995 %
5	50	99.995 %
6	6.6×10^2	99.934 %
7	1×10^2	99.99 %
8	6.2×10^2	99.94 %
9	0	100 %
10	0	100 %
11	10	99.999 %
12	0	100 %
13	25	99.997 %
14	1.5×10^2	99.98 %
15	7.6×10^2	99.92 %
16	0	100 %

Example 33:

Solutions of the examples set forth below are tested for effectiveness against Acanthamoeba castelanii as follows: A 10^7 cyst pellet is dissolved in 10 ml of test solution to result in a 10^6 cyst/ml concentration in test solution. At the times specified below, 1 ml is withdrawn and diluted with 49 ml of saline to result in a cyst concentration of 2×10^4 cyst/ml. 0.1 ml of this diluted solution is then added to 10 ml of nutrient media so that the entire nutrient media begins with a 2×10^3cyst population. The inoculated nutrient media are

cultured for 3 weeks at which point effectiveness is assessed as (a) total kill (-) or (b) partial or no kill (+). The results are reported in Table 6 below.

Table 6:

Solution Example No.	Exposure Time (min.)				
	1	2	3	4	5
9	+	—	—	—	—
19	+	—	—	—	—
17	—	—	—	—	—
21	+				—
22	+				—
23	+				—
24	+				—
25	+				—
26	+				—
27	—				—
28	—				—
29	+				—
30	+				—
31	+				—

Claims

1. A disinfecting and cleaning composition comprising

a) x % by weight of a C_{3-6}alkylene glycol, and

y % by weight of a C_{2-6}alkanol

wherein x and y each independently are zero to about 50 with the proviso that $x/10 + y/2 \geq 1.0$;

b) an amount of a tonicity builder sufficient to raise the solution tonicity to at least the equivalent of a 5 % by weight sodium chloride solution;

c) 0 % to about 25 % by weight of a compatible surfactant;

d) 0 % to about 2 % by weight of a pH adjusting or regulating agent;

e) 0 % to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent; and

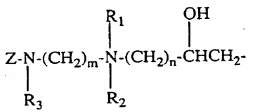
f) the balance of a suitable solvent which is preferably water.

2. The composition of claim 1 wherein said surfactant is selected from

ca) compounds of formula I

$(AmSur\text{-}O)_3\text{-}P=O$ (I)

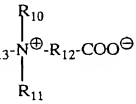
wherein the group AmSur is of the formula



(IA)

wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is an alkanoyl of 6-18 carbon atoms or Z together with R_1 and R_2 is a carbon substituted by C_{5-17}alkyl; and n and m are each independently 1 to 4;

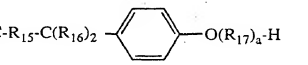
cb) compounds of the formula



(VII)

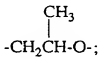
wherein R_9 is alkyl of 5-17 carbon atoms or a C_{6-20}alkanoylamino; each of R_{10} and R_{11} is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl; R_{12} is an alpha,omega-alkylene of 1 to 6 carbons which is unsubstituted or substituted by lower alkyl, hydroxy, or hydroxy lower alkyl; and R_{13} is alpha,omega-C_{1-5}alkylene;

cc) compounds of the formula



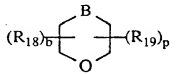
(VIII)

wherein each R_{14} and each R_{16} is independently C_{1-4}alkyl; R_{15} is C_{1-4}-alpha,omega-alkylene; each R_{17} is independently $-CH_2CH_2O-$, $-CH_2CH_2CH_2O-$, or



and a is 3-18; and

cd) compounds of the formula



(IX)

wherein B is a C_{1-4}alpha,omega-alkylene; p is an integer from 0 to (d-1); b is an integer which is (d-p-1); d is 4 to 7; each R_{18} is independently H or a C_{1-4}alkyl which is unsubstituted or substituted by at least one R_{19}; each R_{19} is independently hydroxy which is free, etherified by R_{20}, or esterified by R_{21}; each R_{20} is a C_{2-4} straight or branched oxyalkylene or poly(C_{2-4} straight or branched oxyalkylene), the terminal oxygen of which is bound to H or R_{21}; and each R_{21} is independently an acyl of a C_{2-24}alkanoic acid or a C_{4-24}alkenoic acid; provided that in each compound of formula IX there is at least one free hydroxy group, and at least one R_{21} group.

3. The composition of claim 1 which is a topical medicinal composition, a cosmetic, a facial cleanser, a surgical soap, a shampoo, a household disinfectant, or an industrial disinfectant.

4. The composition of claim 1 which is a contact lens polymer material cleaning and disinfecting solution comprising

a) x % by weight of a C_{3-8}alkylene glycol, and

y % by weight of a C_{2-6}alkanol

wherein x and y each independently are zero to about 50 with the proviso that $x/10 + y/2 \geq 1.0$;

b) an amount of a tonicity builder sufficient to raise the solution tonicity to at least the equivalent of a 5 weight sodium chloride solution;

c) 0 % to about 25 % by weight of an ophthalmic device material compatible surfactant;

d) 0 % to about 2 % by weight of a pH adjusting or regulating agent;

e) 0 % to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent; and

f) the balance of a suitable solvent which is preferably water.

5. The solution of claim 4 wherein y is zero to about 30 and comprising 0 to about 15 % by weight of said surfactant.

6. The solution of claim 4 comprising

a) about 10 % to about 50 % by weight of a C_{3-8}alkylene glycol and about 2 % to about 30 % by weight of a C_{2-6}alkanol;

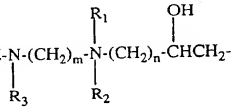
b) an amount of an ophthalmically acceptable alkali metal or alkaline earth metal halide, phosphate, carbonate, or sulfate which is sufficient to raise the solution tonicity to a 5 % to 20 % by weight sodium chloride solution;

c) 0 % to about 15 % of an ophthalmic device material compatible surfactant selected from

ca) compounds of formula I

$(AmSur\text{-}O)_3\text{-}P=O$ (I)

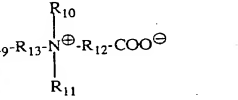
wherein each group AmSur is independently of the formula



(IA)

wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is an alkanoyl of 6-18 carbon atoms or Z together with R_1 and R_2 is a carbon substituted by C_{5-17}alkyl; and n and m are each independently 1 to 4;

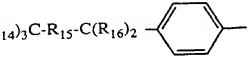
cb) compounds of the formula



(VII)

wherein R_9 is alkyl of 5-17 carbon atoms or a C_{6-20}alkanoylamino; each of R_{10} and R_{11} is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl; R_{12} is an alpha,omega-alkylene of 1 to 6 carbons which is unsubstituted or substituted by lower alkyl, hydroxy, or hydroxy lower alkyl; and R_{13} is alpha,omega-C_{1-5}alkylene;

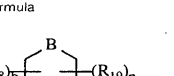
cc) compounds of the formula



(VIII)

wherein each R_{14} and each R_{16} is independently C_{1-4}alkyl; R_{15} is C_{1-4}-alpha,omega-alkylene; each R_{17} is independently $-CH_2CH_2O-$, $-CH_2CH_2CH_2O-$, or

and a is 3-18; and
cd) compounds of the formula



(IX)

wherein B is a C_{1-4}-alpha,omega-alkylene; p is an integer from 0 to (d-1); b is an integer which is (d-p-1); d is 4 to 7; each R_{18} is independently H or a C_{1-4}alkyl which is unsubstituted or substituted by at least one R_{19}; each R_{19} is independently hydroxy which is free, etherified by R_{20}, or esterified by R_{21}; each R_{20} is a C_{2-4}straight or branched oxyalkylene or poly(C_{2-4}straight or branched oxyalkylene), the terminal oxygen of which is bound to H or R_{21}; and each R_{21} is independently an acyl of a C_{2-24}alkanoic acid or a C_{4-24}alkenoic acid; provided that in each compound of formula IX there is at least one free hydroxy group, and at least one R_{21} group;
or poloxamers, reverse poloxamers, meroxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycol-buteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, ceteareths, NTA salts, EDTA salts, and pentetate salts;

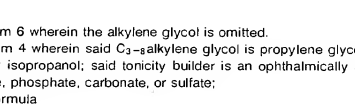
d) 0 % to about 2 % by weight of a pH adjusting or regulating agent selected from i) phosphoric acid, boric acid, lactic acid and citric acid, ii) an ophthalmically acceptable salt thereof, iii) a mixture of said acid and said salt of said acid, iv) an ophthalmically acceptable inorganic acid and v) an ophthalmically acceptable inorganic base;

e) 0 % to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent selected from hydroxy-lower alkyl-cellulose, hydroxy-lower alkanoyl cellulose, lower alkyl-cellulose, lower alkanoyl cellulose, carboxy-lower alkyl-cellulose, poloxamers, reverse poloxamers, meroxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycol-buteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, ceteareths, NTA salts, EDTA salts, and pentetate salts; and

f) water.

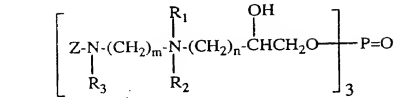
7. The solution of claim 6 wherein the alkylene glycol is omitted.

8. The solution of claim 4 wherein said C_{3-8}alkylene glycol is propylene glycol or hexylene glycol; said C_{2-6}alkanol is ethanol or isopropanol; said tonicity builder is an ophthalmically acceptable alkali metal or alkaline earth metal halide, phosphate, carbonate, or sulfate;
said surfactant is of the formula



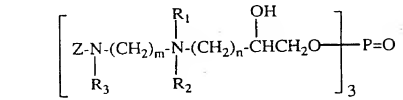
wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is C_{6-18}alkanoyl or Z, together with R_1 and R_2, is a carbon substituted by C_{5-17}alkyl, and n and m are each 1 to 4, in association with sufficient ions of counter charge to result in a net compound charge of zero;
said pH adjusting or regulating agent is selected from i) phosphoric acid, boric acid, lactic acid and citric acid, ii) an ophthalmically acceptable salt thereof, iii) a mixture of said acid and said salt of said acid, iv) an ophthalmically acceptable inorganic acid and v) an ophthalmically acceptable inorganic base;
said viscosity enhancer is selected from hydroxy-lower alkyl-cellulose, hydroxy-lower alkanoyl cellulose, lower alkyl-cellulose, lower alkanoyl cellulose, and carboxy-lower alkyl-cellulose.

9. The solution of claim 6 wherein said C_{3-8}alkylene glycol is propylene glycol or hexylene glycol; said C_{2-6}alkanol is ethanol or isopropanol; said tonicity builder is sodium chloride;
said surfactant is of the formula



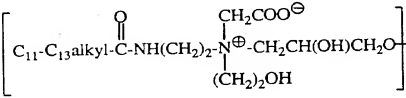
wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is C_{6-18}alkanoyl or Z, together with R_1 and R_2, is a carbon substituted by C_{8-17}alkyl, and n and m are each 1 to 4, in association with sufficient ions of counter charge to result in a net compound charge of zero; said pH adjusting agent is selected from hydrochloric or lactic acid; and said viscosity enhancer is selected from poloxamer 407 and poloxamer 101.

10. The solution of claim 7 wherein said C_{2-6}alkanol is ethanol or isopropanol; said tonicity builder is sodium chloride;
said surfactant is of the formula

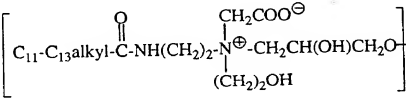


wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is C_{6-18}alkanoyl or Z, together with R_1 and R_2, is a carbon substituted by C_{8-17}alkyl, and n and m are each 1 to 4, in association with sufficient ions of counter charge to result in a net compound charge of zero; said pH adjusting agent is selected from hydrochloric or lactic acid; and said viscosity enhancer is selected from poloxamer 407 and poloxamer 101.

11. The solution of claim 9 wherein said surfactant is of the formula



12. The solution of claim 4 wherein said C_{3-8}alkylene glycol is propylene glycol; said lower alkanol is isopropyl alcohol; said tonicity builder is sodium chloride; said surfactant is of the formula



said pH adjusting or regulating agent is lactic acid; and said viscosity enhancer is hydroxy ethyl cellulose.

13. The solution of claim 4 wherein said C_{3-8}alkylene glycol is present in an amount of about 21 % by weight; said lower alkanol is present in an amount of about 16 % by weight; said surfactant is present in an amount of about 5 % by weight; said pH adjusting or regulating agent is present in an amount of about 1.1 % by weight; said tonicity builder is present in an amount equivalent to a 12.5 % sodium chloride solution; and said viscosity enhancer is present in an amount of about 0.1 % by weight.

14. The solution of claim 4 comprising 0 to 30 % hexylene glycol, 15 to 20 % isopropanol, 7 to 12 % sodium chloride, 5 to 10 % of Miranol, 5 to 15 % of poloxamer 407 or 101 and water.

15. A method of disinfecting and cleaning a contact lens polymer material comprising rubbing the surface of said polymer material with an effective disinfecting and cleaning amount of a solution of claim 4, followed by rinsing said polymer material with normal saline.

16. The method of claim 15 wherein each surface of said polymer material is rubbed with said solution for about 15 seconds and then the entire polymer material is rinsed with normal saline for about 10 seconds.

17. The method of claim 16 wherein said polymer material is in the form of a contact lens.

18. The method of claim 16 wherein said rinsing step is followed by storing said polymer material in normal saline for about 1 minute.

19. Use of a composition according to any of claims 4 to 14 for disinfecting and cleaning a contact lens polymer material.

20. Method of manufacture of a composition of any of claims 4 to 14 characterized by convenient mixing of the individual components.

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(54) **Disinfecting and cleaning composition.**

(57) A disinfection solution, primarily for use in conjunction with contact lenses is disclosed comprising an amount of a pharmaceutically acceptable ionic salt which is equivalent in ionic strength to at least 5 % w/v sodium chloride, at least one of a C_{2-6}alkanol and a C_{3-8}alkylene glycol, a pharmaceutically acceptable surfactant, optionally a buffer and a viscosity enhancing agent, and water.

EP 0 381 617 A3

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 81 0048

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
E,X	EP-A-0 358 447 (SHERMAN LAB.) * page 5; tables 1,2 * *	1-5	A 61 L 2/00 C 11 D 3/00 C 11 D 3/20
X	US-A-4 510 065 (G. J. SHERMAN) * column 5, line 20 - line 64; claims * *	1-5	
X	GB-A-2 103 642 (BARNES - HIND) * claims * *	1	
Y	EP-A-0 209 192 (ICN PHARMACEUTICALS) * claims * *	1	
Y	EP-A-0 233 842 (CIBA - GEIGY) * claims * *	1	
X	EP-A-0 001 888 (FISONS CORP.) * claims * *	1	
X	US-A-3 367 878 (A. MANKOWICH) * claims * *	1	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5) A 61 L C 11 D

The present search report has been drawn up for all claims

Place of search	Date of completion of search	Examiner
The Hague	20 December 91	GOLLER P.

CATEGORY OF CITED DOCUMENTS

X: particularly relevant if taken alone
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